Request for permission for pharmaceutical industry oral testimony at Idaho Medicaid's P&T Committee meeting on 04/21/2017.

Submission # 1

This request has not been accepted for oral testimony (04/04/2017).

Schneider, Keshia - Medicaid

From: Eide, Tamara J.
Sent: Friday, March 31, 2017 3:34 PM
To: Schneider, Keshia - Medicaid
Cc: Gennrich, Jane
Subject: FW: XARELTO - Submission for Idaho Medicaid - April 21, 2017
Attachments: xarelto - prescribing-information.pdf; Idaho Medicaid Cover Letter 2017.pdf; XARELTO - Idaho Medicaid Submission March 2017.pdf

Check my calculations, but I think this is the last day for submissions.

Tami Eide, Pharm.D., BCPS
Medicaid Pharmacy Program Manager
Idaho Department of Health and Welfare
Tamara.Eide@dhw.idaho.gov
3232 Elder St.
Boise, ID 83705
208-364-1829
800-327-5541 fax

My email has changed to Tamara.Eide@dhw.idaho.gov – please update your contacts as appropriate.

From: Monga, Rebha [OMPUS] [mailto:RMonga@its.jnj.com]
Sent: Friday, March 31, 2017 3:00 PM
To: Eide, Tamara J. <Tamara.Eide@dhw.idaho.gov>
Subject: XARELTO - Submission for Idaho Medicaid - April 21, 2017

Dear Dr. Eide,

We are requesting that the P&T Chairman or their designee permit the enclosed new scientific data on XARELTO® (rivaroxaban) to be presented orally by Mae Kwong, Janssen Scientific Affairs Liaison at the April 21st, 2017 P&T Committee meeting.

Please find attached a cover letter and summary of the new scientific data, including the prescribing information.

Please let me know if you have any questions or need anything additional.

Kind Regards,
Rebha Monga, PharmD
Manager, Medical Information
Medical Information & Services
Janssen Scientific Affairs, LLC
1125 Trenton-Harbourton Rd, B2
Titusville, NJ 08560
Phone: 609.730.6557
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Janssen | Pharmaceutical Companies of Johnson & Johnson

March 31, 2017
Idaho Medicaid
Pharmacy & Therapeutics Committee
Attention: Tami Eide, PharmD
3232 Elder Street
Boise, ID 83705

Dear Dr. Eide:

Thank you for your interest in XARELTO® (rivaroxaban), marketed by Janssen Pharmaceuticals, Inc. The enclosed information has been supplied to you in response to your unsolicited request and is not intended as an endorsement of any usage not contained in the prescribing information.

Response(s):

- XARELTO – Idaho Medicaid Summary - 2017

For complete information, please refer to the enclosed full XARELTO Prescribing Information, including the following sections: **BOXED WARNING(S), INDICATIONS AND USAGE, DOSAGE AND ADMINISTRATION, CONTRAINDICATIONS, WARNINGS AND PRECAUTIONS, and ADVERSE REACTIONS.**

If you have any additional questions, please contact us:

- Phone: 1-800-JANSSEN (1-800-526-7736) Monday-Friday, 9:00am-8:00pm
- Web Site: www.janssenmedinfo.com

To report a possible adverse event or product quality complaint, please call the Customer Communications Center immediately, at 1-800-JANSSEN (1-800-526-7736).

Please contact Mae Kwong if you need additional information at Mkwong@its.jnj.com.

Sincerely,

Rebha Monga, PharmD
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XARELTO® (rivaroxaban) Tablets
March 2017

XARELTO® is indicated for treatment of deep vein thrombosis (DVT), treatment of pulmonary embolism (PE), reduction in the risk of recurrence of DVT and of PE following initial 6 months treatment for DVT and/or PE, to reduce the risk of stroke and systemic embolism in patients with nonvalvular atrial fibrillation (NVAF), and for prophylaxis of DVT, which may lead to PE in patients undergoing hip or knee replacement surgery. [1]

Real World Evidence Supports Safety and Efficacy of Rivaroxaban in Nonvalvular Atrial Fibrillation (NVAF)

Post-marketing Safety Surveillance Study (PMSS):

- A 5-year post-marketing safety surveillance study was conducted to gather safety data for rivaroxaban in patients with NVAF.[2] Electronic medical records from the U.S. Department of Defense database were reviewed to assess patients for major bleeding (MB) hospitalizations among rivaroxaban users.
- The mean $CHADS_2$ score was 3 for those with MB and 2.2 for those without MBA.
- A total of 44,793 rivaroxaban users were identified during the 2.5-year period (1,352 MB events in 1,293 patients).
- The overall MB incidence rate, based on a patient's first MB event, was 2.84 [95% CI 2.69-3.00] per 100 person-years. The most common site of bleeding was GI, followed by intracranial.
- A total of 35 patients in the MB group died during hospitalization, for a fatal bleeding rate of 0.10 per 100 person-years (95% confidence interval [CI]:0.07-0.15). Of the 35 patients who died, 26 (74.3%) had an ICH, and 9 (25.7%) had GI bleeding. These results are generally consistent with the pivotal Phase 3 ROCKET AF trial, which compared rivaroxaban to warfarin in patients with NVAF, and reported an event rate of 3.6 per 100 pt-years.[3]

XANTUS:

- An international, prospective, observational, single-arm cohort study assessed the safety and efficacy of rivaroxaban for stroke prevention in 6784 NVAF patients in routine clinical practice.[4] Mean observation period was 329 days and mean $CHADS_2$ score was 2.0.
- The primary outcome was to assess the safety of rivaroxaban in routine practice, recorded as adverse events (AEs) or serious AE (SAEs), including MB (as defined by the International Society on Thrombosis and Haemostasis [ISTH] criteria), all-cause death, and any other AEs and SAEs. Secondary outcome measures included symptomatic thromboembolic events (stroke, non-central nervous system systemic embolism, transient ischemic attack, and myocardial infarction (MI), and non-MB events).
- The rate of MB, thromboembolic events (stroke, systemic embolism (SE), transient ischemic attack(TIA), MI) and all-cause death were low and increased over time.
- MB occurred in 128 (1.9%) patients [2.1 events per 100 pt-years]. Thromboembolic events occurred in 108 (1.6%) patients [1.8 events per 100-patient years]. Fatal bleeding occurred in 12 (0.2%) patients [0.2 events per 100 patient-years], ICH in 26 (0.4%) patients [0.7 events per 100 patient-years], and GI bleeding in 52 (0.8%) patients [0.9 events per 100 patient years].
- All-cause death occurred in 118 (1.7%) patients [1.9 events per 100 patient-years], with cause of death due primarily to cardiovascular causes (41.5%), followed by cancer (19.5%). 6522 patients (96.1%) did not experience any outcomes of treatment-emergent MB, all-cause death, or stroke/SE.
- Treatment persistence remained high, with a discontinuation rate of 20.1% at the end of 1 year.

DRESDEN NOAC Registry:

- Data from a prospective, non-interventional, German registry evaluated the effectiveness and safety of rivaroxaban in 1204 NVAF patients in daily care.[5]
- During a mean follow-up of 796.2 ± 207.3 days, the combined endpoint of stroke/TIA, SE occurred at a rate of 2.03/100 pt-years in the ITT analysis and at 1.7/100 patient-years in the on-treatment analysis (events within 3 days after last intake).
- On-treatment rates were higher in patients receiving 15 mg rivaroxaban (n=384) once daily (OD) compared with the 820 patients receiving 20 mg (2.7 vs 1.25/100 pt-years, p=0.016).
- On treatment, MB occurred at a rate of 3.0/100 patient-years and significantly more often in patients receiving the 15 mg OD dose compared with the 20 mg OD dose (4.5 vs 2.4/100 patient-years).
- Rivaroxaban treatment discontinuation occurred in a total of 277 patients during follow-up (12.0/100 patient years in KM analysis).

REVISIT- US:

- A retrospective analysis of US MarketScan claims data evaluated the safety and efficacy of newly initiated rivaroxaban or apixaban versus warfarin in NVAF patients.[6] The primary endpoint was FDA Mini-Sentinel-coded ischemic stroke and ICH combined.
- A total of 11,411 patients prescribed rivaroxaban between January 1, 2012 and October 31, 2014 were propensity-score matched to an equal number of warfarin patients.
- Patients were oral anticoagulant naïve adults with NVAF, a baseline CHAsDS2-VASc score ≥2, and ≥180 days of constant prescription and medical coverage. Patients with a history of prior stroke, systemic embolism, or ICH were excluded. Mean $CHADS_2$ score was 1.9 for both groups.
- Rivaroxaban was associated with a significant 47% reduction in ICH (0.49 events/100 pt-years vs. 0.96; HR[95% CI] 0.53 [0.35-0.79]), a non-significant reduction in ischemic stroke (0.54 events/100 pt-years vs. 0.83; HR[95% CI] 0.71 [0.47-1.07]), and a significant 39% reduction (0.95 events/100 pt-years vs. 1.60; HR[95% CI] 0.61 [0.45-0.82]), in the combined endpoint of ICH and ischemic stroke compared to warfarin.
- Apixaban (N=4083) was found to non-significantly reduce the composite of ischemic stroke and ICH (0.89 events/100 pt-years vs. 1.44; HR[95% CI] 0.63[0.35-1.12]). ICH risk was reduced by 62% (0.38 events/100 pt-years vs. 0.97; HR[95% CI] 0.38 [0.17-0.88]), however, the risk of ischemic stroke was numerically increased in patients receiving apixaban versus warfarin (0.56 events/100 pt-years vs. 0.51; HR[95% CI] 1.13 [0.49-2.63]).

Use of Rivaroxaban for Treatment of Cancer-associated Venous Thromboembolic Disease

- As part of the global oncology program that included 9 studies with rivaroxaban (CALLISTO), an analysis was conducted based on clinical guidelines to validate the safety and efficacy of rivaroxaban for use in cancer patients.[7]
- Patients received a full course of rivaroxaban and up to 3 days of parenteral anticoagulation. 200 patients with 6 months of follow-up were included in the analysis (136 patients had PE with or without DVT, 64 patients had proximal, symptomatic lower extremity DVT).
- Recurrent VTE and MB occurred at an incidence of 4.4% (95% CI= 1.4%-7.4%) and 2.2% (95% CI= 0%-4.2%), respectively.
- The incidence of clinically relevant nonmajor bleeding leading to discontinuation of rivaroxaban was 3.8% (95% CI= 1.0%-6.5).

- All-cause mortality occurred at an incidence of 17.6% (95% CI=11.7%-23.0%). There were no deaths related to bleeding.

PIONEER-AF PCI

- PIONEER AF-PCI was a randomized, Phase 3, study that assessed the safety of 2 rivaroxaban treatment strategies and one VKA treatment strategy in patients, who have paroxysmal, persistent, or permanent NVAF and have had a percutaneous coronary intervention (PCI) with stent placement.[8]
- The primary safety endpoint was TIMI clinically significant bleeding events (composite of TIMI major bleeding, minor bleeding, or bleeding requiring medical attention) during the treatment-emergent period (first study drug administration up to 2 days following drug discontinuation through 12 months of therapy). The study was not statistically powered to evaluate the efficacy of these treatment strategies.
- The investigator pre-specified the intended P2Y12 inhibitor (ticagrelor 90 mg BID or prasugrel 10 mg daily or clopidogrel 75 mg daily) and the intended duration of DAPT (1,6,12 months). Low dose ASA was defined as 75-100 mg daily.
- In stented AF patients, rivaroxaban either at a dose of 15 mg daily plus P2Y12 inhibitor monotherapy for one year or rivaroxaban 2.5 mg BID plus 1, 6, or 12 months of DAPT reduced the risk of clinically significant bleeding, all-cause mortality or recurrent hospitalization for adverse events as compared with standard of care VKA plus 1, 6, or 12 months of DAPT.

Updated Prescribing Information Data[1]:

Use of Rivaroxaban In Patients With Renal Impairment and End Stage Renal Disease (ESRD)

While there is no indicated dose for ESRD/HD patients taking XARELTO®, new data from a single-dose PK/PD study is now included in Section 8.7 of the XARELTO® PI:

"Clinical efficacy and safety studies with XARELTO did not enroll patients with ESRD on dialysis. In patients with ESRD maintained on intermittent hemodialysis, administration of XARELTO 15 mg once daily will result in concentrations of rivaroxaban and pharmacodynamic activity similar to those observed in the ROCKET AF study [see Clinical Pharmacology (12.2, 12.3)]. It is not known whether these concentrations will lead to similar stroke reduction and bleeding risk in patients with ESRD on dialysis as was seen in ROCKET AF."

Additionally, Section 5.4 of the XARELTO® PI was revised as follows:

"Periodically assess renal function as clinically indicated (i.e., more frequently in situations in which renal function may decline) and adjust therapy accordingly [see Dosage and Administration (2.3)]. Consider dose adjustment or discontinuation of XARELTO in patients who develop acute renal failure while on XARELTO [see Use in Specific Populations (8.7)]"

REFERENCES:

1. XARELTO® (rivaroxaban) Prescribing Information. Janssen Pharmaceuticals, Inc; Titusville, NJ.
2. Peacock WF, et al. *Ann Emerg Med.* 2016. DOI: 10.1016/j.annemergmed.2016.09.032.
3. Patel MR, et al, *N Engl J Med* 2011;365:883-891.
4. Camm AJ, et al. *European Heart Journal.* doi: 10.1093/eurheartj/ehv466.
5. Hecker J, et al. *Thromb Haemost* 2016; 115: 939–949.

6. Coleman CI, et al. *Med Res Opin*. 2016. doi:10.1080/03007995.2016.1237937.
7. Mantha S, et al. *J Thromb Thrombolysis*. Published Sept 30, 2016. doi: 10.1007/s11239-016-1429-1.
8. Gibson CM, et al. *NEJM*. 2016. doi:10.1056/NEJMoa1611594.